Hyaluronic acid conjugated nanoparticle delivery of siRNA against TWIST reduces tumor burden and enhances sensitivity to cisplatin in ovarian cancer.

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Public Summary:
TWIST protein is critical to development and is activated in many cancers. TWIST regulates epithelial-mesenchymal transition, and is linked to angiogenesis, metastasis, cancer stem cell phenotype, and drug resistance. The majority of epithelial ovarian cancer (EOC) patients with metastatic disease respond well to first-line chemotherapy but most relapse with disease that is both metastatic and drug resistant, leading to a five-year survival rate under 20%. We are investigating the role of TWIST in mediating these relapses. We demonstrate TWIST-siRNA (siTWIST) and a novel nanoparticle delivery platform to reverse chemoresistance in an EOC model. Hyaluronic-acid conjugated mesoporous silica nanoparticles (MSN-HAs) carried siTWIST into target cells and led to sustained TWIST knockdown in vitro. Mice treated with siTWIST-MSN-HA and cisplatin exhibited specific tumor targeting and reduction of tumor burden. This platform has potential application for overcoming clinical challenges of tumor cell targeting, metastasis and chemoresistance in ovarian and other TWIST overexpressing cancers.

Scientific Abstract:
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